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LEUKEMIA: TYPE DIAGNOSIS BY OXYDASE METHOD OF BLOOD-STAINING.

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There are two types of leukemia, the lymphatic and myelogenous, the diagnosis of which is based on doubtful clinical and hematological grounds. It is said that in lymphatic leukemia the lymph glands are enlarged out of proportion to the spleen, while in splenomyelogenous leukemia the splenic enlargement is more prominent. This is only true in a certain number of cases. When judgment of type is based on such clinical data, disappointment will often be encountered, due to obtaining blood-findings, which disagree.

In late years more confidence has been placed on the examination of stained blood smear. This is a helpful means, but is uncertain, too, for there are many questions among observers in regard to differentiation between lymphocytes and myelocytes. The simple statement that the myelocytes are granular and the large lymphocytes non-granular is a good working foundation, but the difficulty is in the recognition of the granules by the ordinary methods of staining. There are, fortunately, some blood smears that stain beautifully by a good fresh Wright stain, and no hesitation is made in deciding which is a granular or non-granular cell. Leaving aside the remainder of the findings in a blood examination of leukemia the distinction between the large lymphocytes and myelocytes is of

greatest importance. In order to do this the best plan is to stain all blood smears from cases of leukemia by the oxydase method.

In the use of the oxydase method, alpha-napthol and dimethyl-para-phenylendiamin are brought together in the presence of an oxidizing agent which is present in the leukocytes. An alkaline media is required. When this is done a rapid precipitation of indophenol blue occurs which produces blue granular staining of their protoplasm. The reaction is given by neutrophil, eosinophil and basophil leukocytes and by myelocytes in bone-marrow and leukemic blood. The reaction is not given by lymphocytes nor red blood cells. The method is as follows: Solutions required:

Solution *A*.

95 per cent. alcohol	9 parts
Formaldehyde solution (40 per cent. gas)	1 part

Solution *B*.

Alpha-naphtol (Merck's reagent)	1 gram
40 per cent. alcohol	100 c.c.
Hydrogen peroxide (Must be fresh.)	0.2 c.c.

Solution *C*.

Pyronin	1 gram
Anilin	4 c.c.
40 per cent. alcohol	96 c.c.

Solution *D*.

0.5 per cent. solution of methylene blue (Grubler's BX).

Directions. The films should be fixed by covering with solution *A*. After two minutes this is washed off with water and film flooded with solution *B*. This is washed off and the film is allowed to remain in a dish of running water for fifteen minutes. It is then dried and stained for two minutes with solution *C*. This is washed off with water and solution *D* is poured on and allowed to remain for thirty to sixty seconds. After washing with water the slide is blotted and mounted in neutral balsam.

Results: All myeloid cells, polynuclear myelocytes, transitional and myeloblasts, will show blue granules, while lymphocytes and lymphoblasts will not.

Caution: Solution *B* deteriorates very rapidly and must be made up fresh.

A leukemia case, the physical findings of which were not conclusive, was carefully studied by three separate hematologists. A brief summary of the findings will be of interest, as it shows the different interpretations placed upon cells observed stained by different methods within short periods of time:

A child, aged six years, was first seen October 12, 1919, with chief complaint of weakness. Mucous membranes were pale, a petechial rash that later changed to purpuric spots and general glandular

enlargement was present, including the spleen. The blood findings were as follows:

Red blood cells	2,140,000 Per c.mm.
White blood cells	51,000 "
Hemoglobin	40.0 per cent.

250 cells were counted on a slide stained by the oxydase method with following results:

Polymorphonuclears (neutro)	46.0 per cent.
Large lymphocytes	13.0 "
Small lymphocytes	4.0 "
Myelocytes (neutro)	31.0 "
Mast cells	6.0 "

Many nucleated red cells were seen, the larger number of megaloblastic type. Moderate achromia, polychromatophilia, poikilocytosis and anisocytosis were present.

The blood was examined in another laboratory a few days later which corroborated the diagnosis of myelogenous leukemia and reported the following findings:

Red blood cells	2,400,000 per c.mm.
White blood cells	48,000 "
Hemoglobin	48.0 per cent.
Polymorphonuclears (neutro)	59.4 "
Eosinophils	0.4 "
Large lymphocytes	2.8 "
Small lymphocytes	10.2 "
Transitionals	0.4 "
Myeloblasts	6.4 "
Myelocytes (neutro)	20.4 "

Achromia, anisocytosis, polychromatophilia and poikilocytosis was present. Platelets normal. Six megaloblasts and five normoblasts were seen in making the count of 250 cells.

Three days later another laboratory made an examination of the blood and stained the smear by Wright's method and submitted a diagnosis of lymphatic type from the following findings:

Red blood cells	2,192,000 per cmm.
White blood cells	74,000 "
Hemoglobin	30.0 "
Polymorphonuclears (neutro)	50.0 per cent.
Large lymphocytes	27.0 "
Small lymphocytes	14.0 "
Transitionals	1.0 "
Myelocytes	8.0 "

Irregularities in form were noted with abnormal red cells.

In the last examination it will be noted that a diagnosis of lymphatic leukemia was made from the blood findings. This was based on the finding of myelocytes of vanishing quantity. It is probable the method of staining had a great deal to do with the failure to recognize more myelocytes, as the two previous examiners had found them present in sufficient quantity by the oxydase method to make a diagnosis of lymphatic type. There are fluctuations in blood pictures to be sure, and cases are reported in which one type

has changed to another. The information relative to the latter cases is very meager. Then there is the question of individual observation over which there is no control. It is hoped the evidence submitted will encourage the use of the oxydase method of staining the blood smear to ensure a more accurate distinction between large lymphocytes and myelocytes.

Conclusions. 1. The distinction between lymphocytes and myelocytes by granules in the protoplasm is uncertain by the average examiner with ordinary methods of blood-staining and is liable to render his percentage proportions of these two cells inaccurate. This will result in incorrect type diagnosis of leukemia.

2. The oxydase method of staining the blood smear will be of assistance in making the distinction.

3. A description of a satisfactory method is given.

4. Summarized blood-findings are given which illustrate a possible error in failure to recognize myelocytes by simple method of staining.

I wish to express my thanks to Dr. John Phillips for the opportunity of making examinations of case reported.

THE CURABILITY OF TUBERCULOUS MENINGITIS.

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It is now generally accepted that tuberculosis is a curable disease. The struggle against tuberculosis is based in large measure on the fact of its curability, the effort being to secure as favorable circumstances as possible for the infected in order to bring the process to a standstill and cure. Examples of the cure of tuberculosis are numerous even when the very many latent tuberculous foci, particularly in the lungs and lymph nodes, that are cured spontaneously, are disregarded. Thus tuberculosis of lymph nodes in most cases cures itself without giving rise to any clinical phenomena of note, and this occurs in the lymph nodes of the neck, the chest and the abdomen as well as elsewhere. This is also true of tuberculous processes in the skin, mucous membrane, bones and joints. At the postmortem table one may see complete recovery even of the most extensive and destructive forms of tuberculosis of the bones. At the same time such processes may remain latent and encapsulated, but not healed, through years and years, as, for instance, the case of latent tuberculous spondylitis of twenty years' standing that I observed.

The curability of pulmonary tuberculosis is the corner-stone on which rests all our efforts against tuberculosis with the expenditure